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APPLICATION NO. FILING DATE		FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.	
09/996,015	11/28/2001	Kerry E. Quinn	15966-581CIP (Cura-81 CIP	2939	
7590 01/27/2005			EXAMI	NER	
JENELL LAW	/SON	RAMIREZ, DELIA M			
INTELLECTUA	AL PROPERTY				
CURAGEN CO	RPORATION	ART UNIT	PAPER NUMBER		
555 LONG WH	ARF DRIVE	1652	1652		
NEW HAVEN,	CT 06551	DATE MAILED: 01/27/2005			

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary		Application	Application No. App		pplicant(s)			
		09/996,0	15	QUINN ET AL.				
		Examine		Art Unit				
		Delia M. F		1652				
ہ۔۔ Period for F	The MAILING DATE of this communication application app	ppears on the	cover sheet with the c	orrespondence a	ddress			
THE MA - Extension after SIX - If the per - If NO per - Failure to Any reply	TTENED STATUTORY PERIOD FOR REP ILING DATE OF THIS COMMUNICATION as of time may be available under the provisions of 37 CFR 1 (6) MONTHS from the mailing date of this communication. iod for reply specified above is less than thirty (30) days, a re iod for reply is specified above, the maximum statutory perion reply within the set or extended period for reply will, by statu- or received by the Office later than three months after the mail atent term adjustment. See 37 CFR 1.704(b).	I. 1.136(a). In no eveply within the stated will apply and wute, cause the app	ent, however, may a reply be timutory minimum of thirty (30) days ill expire SIX (6) MONTHS from lication to become ABANDONE	nely filed s will be considered time the mailing date of this of D (35 U.S.C. § 133).				
Status								
1)⊠ R€	esponsive to communication(s) filed on 04	November 0	<u>404</u> .					
2a) <u></u> ⊤r	) This action is <b>FINAL</b> . 2b) ☑ This action is non-final.							
-	Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i> , 1935 C.D. 11, 453 O.G. 213.							
Disposition	of Claims							
4a 5)□ Cl 6)⊠ Cl 7)□ Cl	aim(s) <u>1 and 5-43</u> is/are pending in the app ) Of the above claim(s) <u>5-28,30,31 and 33-</u> aim(s) is/are allowed. aim(s) <u>1,29,32</u> is/are rejected. aim(s) is/are objected to. aim(s) are subject to restriction and	.43 is/are with		ition.				
Application	Papers							
10)□ Th Ap Re	e specification is objected to by the Examire drawing(s) filed on is/are: a) acception and applicant may not request that any objection to the placement drawing sheet(s) including the correct oath or declaration is objected to by the Example.	ccepted or b) le drawing(s) bection is requir	ne held in abeyance. See ed if the drawing(s) is obj	e 37 CFR 1.85(a). ected to. See 37 C	` '			
Priority und	ler 35 U.S.C. § 119							
12) Ac a) 2. 1. 2. 3.	knowledgment is made of a claim for foreig All b) Some * c) None of: Certified copies of the priority docume	nts have beents have beents have beentouries in the comments of the comments and (PCT Rules).	n received. n received in Application ents have been receive e 17.2(a)).	on No ed in this National	Stage			
Attachment(s)								
2)  Notice of 3)  Informati	References Cited (PTO-892)  Draftsperson's Patent Drawing Review (PTO-948) on Disclosure Statement(s) (PTO-1449 or PTO/SB/06 o(s)/Mail Date 5/22/02,7/18/02.	8)	<ul> <li>Interview Summary Paper No(s)/Mail Da</li> <li>Notice of Informal P</li> <li>Other: <u>alignments</u>.</li> </ul>	ite	O-152)			

#### **DETAILED ACTION**

## Status of the Application

Claims 1, 5-43 are pending.

Applicant's election without traverse of Group II, claims 1-4, 29, 32 drawn in part to the polypeptide of SEQ ID NO: 6, amendment of claim 1, and cancellation of claims 2-4, in a communication filed on 11/4/2004 are acknowledged.

Claims 5-28, 30, 31 and 33-43 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

# Inventorship

1. In view of the papers filed 11/4/2004, the inventorship in this nonprovisional application has been changed by the deletion of inventors Mario W. Leite, Li Li and Steven K. Spaderma.

The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of the file jacket and PTO PALM data to reflect the inventorship as corrected.

#### Specification

2. The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. See particularly page 2, line 31 of the specification. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

Application/Control Number: 09/996,015 Page 3

Art Unit: 1652

# **Priority**

3. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 119(e) to provisional application No. 60/175,534 filed on 01/11/2000, 60/159,613 filed on 10/14/1999, and 60/224,086 filed on 08/09/2000.

- 4. Acknowledgment is made of a claim for domestic priority under 35 U.S.C. 120 or 121 to US application No. 09/641,741 filed on 08/18/2000.
- 5. SEQ ID NO: 6 appears to have been first disclosed in U.S. Provisional Application No. 60/224,086 filed on 8/9/2000.

# Information Disclosure Statement

6. The information disclosure statements (IDS) submitted on 5/22/2002 and 7/18/2002 are acknowledged. The submissions are in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statements are being considered by the examiner.

# Claim Objections

7. Claim 1 is objected to due to the recitation of "(c) the amino acid sequences given by SEQ ID NO: 6". For clarity and consistency, the term should be replaced with "(b) the amino acid sequence given by SEQ ID NO: 6". Appropriate correction is required.

# Claim Rejections - 35 USC § 112, Second Paragraph

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Application/Control Number: 09/996,015 Page 4

Art Unit: 1652

9. Claims 1, 29 and 32 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

10. Claim 1 (claims 29 and 32 dependent thereon) is indefinite in the recitation of "mature form of the amino acid sequence given by SEQ ID NO: 6" for the following reasons. First, it is unclear as to what is a mature form of a sequence. As known in the art, sequences are graphical representations of the order in which nucleotides/amino acids are arranged in a molecule. Therefore, it is unclear as to what constitutes the mature form of a graphical representation. In addition, even if the term "mature form" refers to a polypeptide, and not a sequence, it is noted that while one of skill in the art would interpret the term "mature form" as referring to a polypeptide lacking a signal peptide or the N-terminal methionine, the specification describes the term "mature form" (page 22, lines 13-25), as one which encompasses not only a polypeptide lacking its signal peptide or the N-terminal methionine but a polypeptide subjected to any proteolytic cleavage event. As such, it is unclear if the intended meaning of the term is that generally used in the art or if the term encompasses any fragment of the polypeptide recited in the claim. It is suggested that the claim be amended to recite the specific amino acid residues which correspond to the desired fragment of the polypeptide of SEQ ID NO: 6 ("amino acids X-Y of the amino acid sequence given by SEQ ID NO: 6", or similar). For examination purposes, the claim will be interpreted as being directed in part to a polypeptide comprising any fragment of the polypeptide of SEQ ID NO: 6. Correction is required.

# Claim Rejections - 35 USC § 101

#### 11. 35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Art Unit: 1652

12. Claims 1, 29 and 32 rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a substantial and specific asserted utility or a well established utility.

Page 5

Claims 1, 29 and 32 are drawn to (1) the polypeptide of SEQ ID NO: 6, (2) polypeptides comprising any fragment of (1), and (3) compositions comprising (1) or (2).

Applicants refer to the polypeptide of SEQ ID NO: 6 as an aortic carboxypeptidase-like protein 2 (ACPL2; page 3, Summary of the Invention) and indicate that the polypeptides of the invention have sequence similarity to previously described members of the carboxypeptidase family. Applicants also indicate that the polypeptide of SEQ ID NO: 6 is highly homologous to a 734 amino acid long human protein, which in turn is moderately similar to a mouse metallocarboxypeptidase CPX-1. While Applicants have asserted a biological function for the polypeptide of SEQ ID NO: 6 as that of an aortic carboxypeptidase-like protein, the claimed invention does not meet the utility requirements for the following reasons. As noted in the specification (pages 1-2 of the specification), carboxypeptidases are involved in multiple biological processes and are very diverse. However, the specification fails to provide any clue as to (1) the specific biological function of the polypeptide of SEQ ID NO: 6, (2) the biological processes associated with the polypeptide of SEQ ID NO: 6, (3) disorders/diseases which are associated with the expression, or lack thereof, of the polynucleotide of SEQ ID NO: 5 (encodes the polypeptide of SEQ ID NO: 6), or (4) which are the substrates/targets of the alleged aortic carboxypeptidase-like protein. Furthermore, it is noted that as indicated in the specification (page 11, last paragraph, page 12, line 1), the ACPL proteins of the invention may lack enzymatic cleavage function (i.e. carboxypeptidase activity) since they appear to lack several active site residues which are important for catalytic activity. Layne et al. (J.Biol. Chem. 273(25):15654-15660, 1998; cited in the specification; page 11, Table I) discloses a human aortic carboxypeptidase-like protein which has a carboxypeptidaselike domain of approximately 500 amino acids at its C-terminus but lacks carboxypeptidase activity (page 15659, left column, second paragraph), and suggest that while it may be catalytically inactive, it can bind

Art Unit: 1652

to other proteins via the carboxypeptidase-like domain. Layne et al. also disclose that the human aortic carboxypeptidase-like protein plays a role in differentiated vascular smooth cells (Abstract, last sentence). Since (1) according to the specification and the teachings of Layne et al., an aortic carboxypeptidase-like protein may not be active as a carboxypeptidase, (2) the specification is completely silent as to any additional non-enzymatic function associated to the polypeptide of SEQ ID NO:6, such as those indicated by Layne et al. in regard to their protein, and (3) there is no clue as to the specific function of the closest structural homolog (SPTREMBL Q9NUB5, also labeled Q96SM3) other than being described as being a CPX-1 homolog with no carboxypeptidase activity (see attached alignment of Q96SM3 against the polypeptide of SEQ ID NO:6; immediately after the last literature citation under "Function"), one of skill in the art cannot determine the actual biological function of the claimed polypeptide.

Page 6

Applicant's asserted utility for the polypeptide of SEQ ID NO: 6 (aortic carboxypeptidase-like protein), particularly in view of a lack of knowledge as to its specific biological function, the biological processes associated with the polypeptide of SEQ ID NO: 6, disorders/diseases which are associated with the abnormal expression of the polynucleotide of SEQ ID NO: 5, or the substrates/targets associated with the polypeptide of SEQ ID NO: 6, is not specific or substantial since it will require or constitute carrying out further research to identify or reasonably confirm a "real world" context of use. See e.g., Brenner v. Manson, 383 U.S. 519, 148 USPQ 689 (Sup. Ct. 1966). The instant situation is analogous to the lack of substantial utility examples provided by MPEP § 2107.01 in that basic research is required to study the properties of the claimed polypeptides as well as the mechanisms in which the claimed polypeptides are involved. Since the instant specification does not disclose an specific and substantial "real world" use for the polypeptide of SEQ ID NO: 6, then the claimed invention as disclosed does not meet the requirements of 35 U.S.C. §101 as being useful.

Art Unit: 1652

13. Claims 1, 29 and 32 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

# Claim Rejections - 35 USC § 112, First Paragraph

14. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 1, 29 and 32 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1, 29 and 32 are directed in part to a polypeptide of any function comprising any fragment of the polypeptide of SEQ ID NO: 6, and compositions thereof. See Claim Rejections under 35 USC 112, second paragraph for claim interpretation. While the specification discloses the structure of the polypeptide of SEQ ID NO: 6 and indicates that said polypeptide is an aortic carboxypeptidase-like protein (ACPL) 2, the specification fails to disclose the structure and function of other polypeptides comprising any fragment of the polypeptide of SEQ ID NO: 6. The genus of polypeptides claimed is a large variable genus with the potentiality of encompassing many different functions. As taught by the art, even highly structurally homologous species may not share the same function. Witkowski et al. (Biochemistry 38:11643-11650, 1999) teaches that one amino acid substitution transforms a β-ketoacyl synthase into a malonyl decarboxylase and completely eliminates β-ketoacyl synthase activity. Seffernick et al. (J. Bacteriol. 183(8):2405-2410, 2001) teaches that two naturally occurring Pseudomonas

Art Unit: 1652

enzymes having 98% amino acid sequence identity catalyze two different reactions: deamination and dehalogenation, therefore having different function. Therefore, the claimed genera of polypeptides have the potentiality of encompassing many different functions.

Page 8

In addition, while a sufficient written description of a genus of polypeptides may be achieved by a recitation of a representative number of polypeptides defined by their sequence or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus, in the instant case, the interpreted structural feature, "any fragment of SEQ ID NO: 6", does not constitute a substantial portion of the genus as the remainder of any polypeptide comprising said structural elements is completely undefined and the specification does not define the remaining structural features for members of the genus to be selected. Many functionally and structurally unrelated polypeptides are encompassed by these claims. The specification only discloses a single species of the claimed genus which is insufficient to put one of ordinary skill in the art in possession of all attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

16. Even if specific and substantial utility or well established utility is found for the polypeptide of SEQ ID NO: 6, the following rejection applies. Claims 1, 29 and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the polypeptide of SEQ ID NO: 6, and the polypeptide of SEQ ID NO: 6 lacking its N-terminal Met residue or its signal peptide, does not reasonably provide enablement for (1) a polypeptide of any function comprising any fragment of the polypeptide of SEQ ID NO: 6, (2) a pharmaceutical composition comprising the polypeptide of SEQ ID NO: 6, or (3) a pharmaceutical composition comprising a polypeptide of any function comprising any fragment of the polypeptide of SEQ ID NO: 6. The specification does not enable any person skilled in

Art Unit: 1652

the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The criteria for undue experimentation, summarized in *re Wands*, 8, USPQ2nd 1400 (Fed. Cir. 1988) are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented, 3) the presence and absence of working examples, 4) the nature of the invention, 5) the state of prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breath of the claims.

The scope of the claims is not commensurate with the enablement provided in regard to the extremely large number of polypeptides of unknown function and structure encompassed by the claims, as well as unknown diseases which can be treated with said polypeptides. As indicated above, while the specification discloses the structure of the polypeptide of SEQ ID NO:6 and indicates that this polypeptide is an aortic carboxypeptidase-like protein (ACPL) 2, the specification is completely silent in regard to (1) the structures and functions of all the polypeptides comprising any fragment of the polypeptide of SEQ ID NO: 6, (2) which fragments of the polypeptide of SEQ ID NO: 6 are required in any polypeptide such that it can display the same function as that of the polypeptide of SEQ ID NO: 6, and (3) diseases that can be effectively treated using a "pharmaceutical composition" comprising the claimed polypeptides.

While one could argue that the genus of polypeptides comprising any fragment of the polypeptide of SEQ ID NO: 6 is enabled since one could make those polypeptides, as indicated above, the state of the art teaches the unpredictability of assigning function based solely on structural homology and discloses examples of how even small structural changes can lead to major changes in function. See the teachings of Seffernick et al., and Witkowski et al. already discussed. Therefore, while one of skill in the art can make these polypeptides, determining the function of such polypeptides without undue experimentation would require some knowledge or guidance as to how structure correlates with the desired function.

In regard to pharmaceutical compositions comprising the recited polypeptides, it is noted that the term "pharmaceutical" implies a treatment of a disease, and based on the information provided in the specification, it is unpredictable as to which diseases can be effectively treated using a "pharmaceutical composition" comprising the claimed polypeptides. Neither the specification nor the prior art provide sufficient guidance as to what specific diseases could be successfully treated by administering a "pharmaceutical composition" comprising the recited polypeptides, and attempting to identify a disease treatable using such a "pharmaceutical composition" would constitute undue experimentation. The specification merely provides a statement indicating that the proteins disclosed in the specification have potential therapeutic applications for treating hypertensive disorders and/or vascular endothelial disorders. (page 19, last paragraph). There is no indication or evidence that administering therapeutic dosages of the polypeptide of SEO ID NO: 6 would have any use in treating these disorders beyond mere speculation. Furthermore, even if the specification had provided sufficient guidance as to a disease treatable by administering a "pharmaceutical composition" comprising the polypeptide of SEQ ID NO:6, the specification provides no guidance as to what, besides such polypeptide, would compose such a composition. Making and testing the infinite number of compositions to find one that is effective would constitute undue experimentation.

Therefore, due to the lack of relevant examples, the amount of information provided, the lack of knowledge about the critical structural elements required to display the desired function, the unpredictability of the prior art in regard to function based on homology, and the lack of knowledge as to the specific diseases which can be treated by pharmaceutical compositions comprising the recited polypeptides, the specific dosages and additional compounds in such composition, one of ordinary skill in the art would have to go through the burden of undue experimentation in order to (1) determine the actual function of any polypeptide comprising any fragment of the polypeptide of SEQ ID NO: 6, (2) determine the specific diseases which can be treated with the polypeptides recited in the claims, and (3) determine

Application/Control Number: 09/996,015 Page 11

Art Unit: 1652

dosage and additional ingredients required in the pharmaceutical compositions claimed. Thus, Applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the invention in a manner reasonably correlated with the scope of the claims.

## Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

- (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
- 18. Claim 1 is rejected under 35 U.S.C. 102(a) as being anticipated by Ota et al. (EMBL accession number BAB55275; TrEMBL accession number Q96SM3; Q9NUB5; May 2001; cited in the IDS).

  Claim 1 (as interpreted) is directed to a polypeptide comprising any fragment of the polypeptide of SEQ ID NO: 6. Ota et al. teaches a protein comprising amino acids 1-509 and 510-574 of the polypeptide of SEQ ID NO: 6, therefore anticipating the instant claim as interpreted. See attached alignment provided for visualization purposes.
  - (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
- 19. Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Layne et al. (J.Biol. Chem. 273(25):15654-15660, 1998; cited in the IDS). Claim 1 (as interpreted) is directed to a polypeptide comprising any fragment of the polypeptide of SEQ ID NO: 6. Layne et al. teaches a human aortic carboxypeptidase-like protein comprising several fragments of the polypeptide of SEQ ID NO: 6, therefore anticipating the instant claim as interpreted. See attached alignment provided for visualization purposes.

Art Unit: 1652

21.

#### Conclusion

Page 12

20. No claim is in condition for allowance.

Certain papers related to this application may be submitted to Art Unit 1652 by facsimile

transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the

notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December

28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be

retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE

SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

22. Information regarding the status of an application may be obtained from the Patent Application

Information Retrieval (PMR) system. Status information for published applications may be obtained from

either Private PAIR or Public PAIR. Status information for unpublished applications is available through

Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC)

at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally

be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Delia M. Ramirez, Ph.D. Patent Examiner Art Unit 1652

DR January 21, 2005 Chordata; Craniata; Vertebrata; Euteleostomi;

Bukaryota; Metazoa; Chordata; Craniata; Vertebrata; Eutele Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.

Homo sapiens (Human)

SEQUENCE FROM N.A. (ISOFORM 1).

NCBI\_TaxID=9606;

Potential carboxypeptidase X precursor (EC 3.4.17.-) (Metallocarboxypeptidase CPX-1).

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                                                 Strausberg R.;
Submitted (DEC-2003) to the EMBL/GenBank/DDBJ databases.
                                                                                                           734 AA; 81693 MW; DSFFC614FE356102 CRC64;
                                                                                                                                          96.9%; Score 2974; DB 2; 78.1%; Pred. No. 7.2e-209;
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Carboxypeptidase.
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RESUBENCE FROM N.A. (120FORM 1).

RESUBENCE FROM N.A. (120FORM 1).

RA CGA T., SUZUKI Y., NISHIKAWA T., OLSUKI T., SUGIYAMA T., ITIE R.,

RA CGA T., SUZUKI Y., NISHIKAWA T., OLSUKI T., SIMULA K., MAKITA H.,

RA GARAMEREU A., HAYASHI K., SATO H., NAGAI K., XIMULA K., MAKITA H.,

RA SEKINE M., ODAYASHI M., NISHI T., SHIDBHARA T., TANAKA T., ISHII S.,

RA MARAMATI K., MUTAKAMA K., YANGA T., ISON Y., NAGARIKA M.,

RA SHIRATOTI A., SUGO H., KAMAI Y., KAWAYAMA T., KIKAWA E.,

RA SHIRATOTI A., SUGO H., KAMAI Y., YOKOI T., FULUYA T., KIKAWA E.,

RA SHIRATOTI K., MATAHASHI M., KATSHI T., YAMASHICA H., MUTAKAWA K.,

RA SMIRATOTI K., TARAHASHI M., WATAHASHI H., MUTAKAWA K.,

RA SMIRATOTI K., TAKAHASHI S., WATAHASHI H., MUTAKAWA K.,

RA SMIRATOTI K., TAKAHASHI S., WATAHASHI H., TANAKAWA K.,

RA ISHIGA S., ONO Y., TAKAHOTI S., WATAHASHA H., TANAKAWA K.,

RA ISHIGA S., ONO Y., TAKAHOTI S., WATAHASHI K., TANAKAWA K.,

RA ISHIGA S., ONO Y., TAKAHOTI S., WATAHASHI K., TANAKAWA S.,

RA INOSE N., WANSAHINI K., YUUKI H., OSHIMA A., SASSAKI N., AACIBUKA S.,

RA MORIYA S., MOMIYAMA H., SATOH N., TAKAMA S., SASSAKI N., AACIBUKA S.,

RA MAKAGAWA S., SENGHO A., MIZOGUCHI H., TANAKAWA S.,

RA MAKAGAWA S., SENGHO A., MIZOGUCHI H., TANAGAMA N., KAWAKAMI B.,

RA PUJIMOTI Y., KOMIYAMA M., TASHIRO H., TANAGAMA M., KAWAKAMI B.,

RA PUJIMOTI Y., KOMIYAMA M., TASHIRO H., TANAGAMA M., SABAKI M.,

RA RABABATA S., SENGH Y., MOGUCHI S., ILOH T., SHIGAT T.,

RA KAWABATA A., HIKIJI T., KODATAKE N., INAKABAMA M., SABAKI M.,

RA RABAMATA K., FUJIMI Y., OZAKKI K., HITAO M., OKAMATA T.,

RA MATSHMIMA Y., MAKAMI T., WOGUCHI S., TAKHARA M., SABAKI M.,

RA MATSHMIMA S., PUJI Y., WATAHA H., WATAHABA M., SABAKI M.,

RA MATSHMIMA S., PUJI Y., WATAHA H., WATAHABA M., SABAKI M.,

RA MATSHMIMA S., PUJI Y., WATAHA M., MATAHA M., MATAHA M., MATAHA M., MATAHA M., MATAHA M., WATAHA M
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MEDLING M., Stavrides G., Almeida J.P., Babbage A.K., Bagguley C.L.,

Rasaley O.P., Bard C.P., Blakey S.E., Bridgeman A.M., Brown A.J.,

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And Mannond S., Harley J.L., Heath P.D., Ho S., Holden J.L., Howden P.J.,

Huckle E., Hunt A.R., Hunt S.E., Jekosech K., Johnson C.M., Johnson D.,

Kay M.P., Kimberley A.M., King A., Knights A., Laird G.K., Lawlor S.,

Lehvaeslaiho M.H., Leversha M.A., Lloyd C., Lloyd D.M., Lovell J.D.,

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Skuce C.D., Smith M.L., Soderlund C., Steward C.A., Sulston J.E.,

Swann R.M., Sycamore N., Taylor R., Thomas D. W., Thorpe A.,

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Swann R.W., Sycamore N., Taylor R., Wallisy D.L., Wallian R.W., Bentley D.R., Williang L., Wi
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"The DNA sequence and co
Nature 414:865-871(2001)
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Last sequence update) Last annotation update)

096SM3; Q9NUB5; 28-FEB-2003 (Rel. 41, Created) 28-FEB-2003 (Rel. 41, Last seque) 05-JUL-2004 (Rel. 44, Last amm

STANDARD;

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                                     A MEDLINE-22388257; PubMed-12477932; DOI=10.1073/pnas.242603899;
A Kausner R.D., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D.,
A Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
A Altschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,
A Hopkins R.F., Jordan H., Moorer T., Max S.I., Wang J., Hsieh F.,
Diatchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,
A Rapleton M., Soares M.B., Bonaldo M.F., Carainori P., Prange C.,
RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Prange C.,
RA Raha S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,
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A Villalon D.K., Murny D.M., Sodergren B.J., Lu X., Gibbs R.A.,
Rhiching M., Madan A., Young A.C., Shevchenko Y., Bouffard G.G.,
A Hakesley R.W., Touchman J.W., Green B.D., Dickson M.C.,
A Blakesley R.W., Touchman J.W., Green B.D., Dickson M.C.,
A Rodriguez A.C., Grimwood J., Schmutz J., Myers R.M.,
Chenertion and initial analysis of more than 15,000 full-length human
an mouse CDNA sequences.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   This SWISS-PROT entry is copyright. It is produced through a collaboration between the Swiss Institute of Bioinformatics and the EMBL outstation the European Bioinformatics Institute. There are no restrictions on its most by non-profit institutions as long as its content is in no way modified and this statement is not removed. Usage by and for commercial entities requires a license agreement (See http://www.isb-sib.ch/announce/or send an email to license@isb-sib.ch).
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     Isoid=Q96SM3-2; Sequence=VSP 000780, VSP 000781; Note=May be produced at very low levels due to a premature stop codon in the mRNA, leading to nonsense-mediated mRNA decay. No experimental confirmation available; SIMILARITY: Belongs to peptidase family M14. SIMILARITY: Contains 1 F5/8 type C domain.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                          PubMed=14759258; DOI=10.1186/gb-2004-5-2-8;
Hillman R.T., Green R.E., Brenner S.E.;
"An unappredated roll for RNA surveillance.";
Genome Biol. 5:RESEARCHO08.1-RESEARCH008.16(2004).
-:- FUNCTION: May be involved in cell-cell interactions. No carboxypeptidase activity was found yet (By similarity).
-:- SUBCELLULAR LOCATION: Secreted (By similarity).
-:- ALTERNATIVE PRODUCTS:
Event=Alternative splicing; Named isoforms=2;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       Proc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    SPLICE ISOFORM(S) THAT ARE POTENTIAL NMD TARGET(S)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           IsoId=Q96SM3-1; Sequence=Displayed;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       InterPro; IPR000859; CarboxypepD_reg.
InterPro; IPR000879; Gal_Dind_like.
InterPro; IPR0008379; Gal_Dind_like.
InterPro; IPR000834; Peptidase_M148.
InterPro; IPR008575; Peptidase_M148.
Pfam; PF00754; F5_F8_type_C; I.
Pfam; PF00754; F5_F8_type_C; I.
Pfam; PF00755; CREOXYPTASEA.
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SMART; SM00631; Zn_pept; 1.

PROSITE; PS00132; CARBOXYPEPT_ZN_1; 1.

PROSITE; PS0123; CARBOXYPEPT_ZN_2; 1.

PROSITE; PS01285; FA58C_1; FALSE_NEG.

PROSITE; PS01286; FA58C_2; FALSE_NEG.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               EMBL; AK027661; BAB55275.1; -.
EMBL; AL035460; CAB82246.1; -.
EMBL; BC032692; AAH32692.1; -.
HSSP; Q90240; 1HBL.
MEROPS; M14.015; -.
Genew; HGNC:15771; CPXM.
FROM N.A. (ISOFORM 2)
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EQHVRIRVIKKKKVIMKKRKKLTLTRPTPLVTAGPLVTPTPAGTLDPAEKQETGCPPLGL 120
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              ESLRVSDSRLEASSSQSFGLGPHRGRLNIQSGLEDGDLYDGAWCAEEQDADPWFQVDAGH 180
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  NYKAMRKLMKQVQEQCPNITRIYSIGKSYQGLKLYVMEMSDKPGEHELGEPEVRYVAGMH 360
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                                                                                                                                                                                                                              N-linked (GlCNAC...) (Potential).
N-linked (GlCNAC...) (Potential).
N-linked (GlCNAC...) (Potential).
N-linked (GLCNAC...) (Potential).
GLINKQVQEQCPNITRIYSIGKSYQGLKLYVMEMSDKPGEHEL
GEPEVRYV -> VRYNPYDLGRRAHPSQVPFPPSHRGTTCC
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    ESLRVSDSRLEASSSQSFGLGPHRGRLNIQSGLEDGDLYDGAWCAEEQDADPWFQVDAGH
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         PTRFSGVITQGRNSVWRYDWVTSYKVQFSNDSRTWWGSRNHSSGMDAVFPANSDFETPVL
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     241 NLLPEPQVARFIRLLPQTWLQGGAPCLRAEILACPVSDPNDLFLEAPASGSSDPLDFQHH
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    421 WAEGRWINGSIDLMHNFADLNTPLWEAQDDGKVPHIVPNHHLPLPTYYTLPNATVAPETR
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1 MWGLLLALAAFAPAVGPALGAPRNSVLGLAQPGTTKVPGSTPALHSSPAQPPAETANGTS
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           361 GNEALGRELLLLLMQFLCHEFLRGNPRVTWLLSEMRIHLLPSMNPDGYEIAYHRGSELVG
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                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   541 LAMQDTSRRPCHSQDFSVHGNIINGADWHTVPGSMNDFSYLHTNCFEVTVELSCDKFPHE
                                                                                                                                                                                                                                                                                                                              DCACMPLLPPDVSAFSPVDP (in isoform 2).
FA58C_3; 1.
ng; Carboxypeptidase; Glycoprotein; Hydrolase;
                                                                                                                                                                                                 N-linked (GICNAC. . .) (Potential)
                                                                                                                                                                                                                                                                                                                                                                                                                                                                     1; Indels 160;
                                                                                                                                                                                                                                                                                                                                                                                                                                     Score 2972; DB 1; Length 734;
Pred. No. 1e-208;
0; Mismatches 1; Indels 160
                                                                                                                     Zinc (By similarity).
Zinc (By similarity).
Zinc (By similarity).
Zinc (By similarity).
Nucleophile (By similarity).
                                                carboxypeptidase
C.
                                                                                                                                                                                                                                                                                                                                                                        /FTId=VSP_000781.
W -> R (in Ref. 2).
815705578E8A58F3 CRC64;
                                                                                                                                                                                                                                                                                                                                                            Missing (In isoform 2)
                                                                                                                                                                                                                                                                                                                                            /FTId=VSP 000780
                                                                                                                                                                                        similarity
                                                             Potential or F5/8 type (Poly-Lys.
                                                                                                                                                                                      Ву
                                                                                                                                                                                                                                                                                                                                                                                                        734 AA; 81697 MW;
                                Metalloprotease; Signal; Zinc
                                                                                                                                                                                                                                                                                                                                                                                                                                     tch 96.8%; al Similarity 78.1%; 573; Conservative (
                                                Alternative splicing;
                                                                                                                                                                                                                                                                                                                                                         357
                                                          METAL
METAL
METAL
ACT SITE
DISULFID
CARBOHYD
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Best Local (
                                                                                                                                                                                                                                  CARBOHYD
                                                                                                                                                                                                                                                                                               VARSPLIC
                                                                          DOMAIN
DOMAIN
DOMAIN
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510

SULT 6 N2E1

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DNA Cell Biol. 18:175-185(1999).
                                                                                                                                                                                                                        Name=Cpxm; Synonyms=Cpxml, Cpxl;
Mus musculus (Mouse).
                                                                                                                                                                                                              (Metallocarboxypeptidase CPX-1)
                                                                                                                                                                                                                                                                                                                                                                                 SEQUENCE FROM N.A.
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    601 NELPQEWENNKDALLTYLEQVRMGIAGVVRDKDTELGIADAVIAVDGINHDVTTAWGGDY 660
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                        -----MYTASAEGYHSVTRNCRVTFEEGPFPCNFVLTKTPKORLRELLAAGAKVPP
                                  Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
Mammalia; Eutheria; Primates; Catarrhini; Hominidae; Homo.
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R GO; GO:0004180; F:carboxypeptidase Activity; IEA.
R GO; GO:0004180; F:carboxypeptidase activity; IEA.
GO; GO:0007155; P:cell adhesion; IEA.
GO; GO:0007155; P:cell adhesion; IEA.
R GO; GO:000508; P:proteolysis and peptidolysis; IEA.
R InterPro; IPR008979; Gal Dind like.
R InterPro; IPR008979; Gal Dind like.
R Pfam; PF00746; PE-FB LYPE-C; I.
R Pfam; PF00746; Zn CarbOpept; 1.
R RINTS; PR00765; CREDXYPTASEA.
R SWART; SW00231; FASEC; 1.
R RMART; SW0031; Zn Dept; 1.
R RMART; SW0031; Zn Dept; 1.
R PROSITE; PS00132; CARBOXYPEPT_ZN_1; 1.
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              477 AA; 52766 MW; 0A3FBE477B57A246 CRC64;
                                                                                                                                                          01-0CT-2002 (TrEMBLrel. 22, Created)
01-0CT-2002 (TrEMBLrel. 22, Last sequence update)
01-0CT-2003 (TrEMBLrel. 25, Last annotation update)
Hypothetical protein PSEC0226.
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                                                                                                                                            477 AA.
                                                                        561 DLRRRLERLRGQKD 574
                                                                                     Matches 464; Conservative
                                                                                                                                               PRELIMINARY;
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SEQUENCE 477 AJ
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KC TISSUE=Breast tumor;

RX MEDLINE=2388257; PubMed=12477932; DOI=10.1073/pnas.242603899;

RA Strausberg R.L., Feingold E.A., Grouse L.H., Derge J.G.,

RA Aluschul S.F., Zeeberg B., Buetow K.H., Schaefer C.F., Bhat N.K.,

RA Altechul S.F., Jordan H., Moore T., Max S.I., Wang J., Hsieh F.,

Batchenko L., Marusina K., Farmer A.A., Rubin G.M., Hong L.,

RA Bigleton M., Soares M.B., Bonaldo M.F., Casavant T.L., Scheetz T.E.,

RA Brownstein M.J., Usdin T.B., Toshiyuki S., Carninci P., Frange C.,

RA Rahas S.S., Loquellano N.A., Peters G.J., Abramson R.D., Mullahy S.J.,

RA Bosak S.A., McKevan P.J., Neckernan K.J., Malek J.A., Gunaratne P.H.,

RA Richards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,

RA Nichards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W.,

RA Millalon D.K., Muzny D.M., Sodergren B.J., Lu X., Gibbs R.A.,

Rahey J., Helton E., Ketteman M., Madan A., Rodrigues S., Sanchez A.,

Rahesley R.W., Toung A.C., Shevchenko Y., Bouffard G.G.,

RA Rodriguez A.C., Grimwood J., Myers R.M.,

Randiguez A.C., Grimwood J., Myers R.M.,

Randiguez A.C., Grimwood J., Salska U., Smailus D.E.,

Randerfield Y.S.N., Kzzywinski M.I., Skalska U., Smailus D.E.,

Randerfield A., Schein J.E., Jones S.J.M., Marra M.A.;

Randiguez A., Schein J.E., Jones S.J.M., Marra M.A.;

Randiguez A., Schein J.E., Jones S.J.M., Marra M.A.;
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NYKAMRKIMKQVQEQCPNITRIYSIGKSYQGLKLYVMEMSDKPGEHELGEPEVRYVAGMH
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                            MEDLINE=99171585; PubMed=10073577;
Lei Y., Xin X., Morgan D., Pintar J.E., Fricker L.D.;
"Identification of mouse CPX-1, a novel member of the
metallocarboxypeptidase gene family with highest similarity to CPX-
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                             Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Buteleostomi;
Mammalia; Eutheria; Rodentia; Sciurognathi; Muridae; Murinae; Mus
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                                                                                                                                                                                                                                                  421 WAEGRWINQSIDLINHNFADLINTPLWEAQDDGKVPHIVPNHHLPLP 465
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Q92100; Q99LA3;
28-FEB-2003 (Rel. 41, Last sequence update)
28-FEB-2003 (Rel. 41, Last annotation update)
65-UTU-2004 (Rel. 44, Last annotation update)
Potential carboxypeptidase X precursor (EC 3.4.17.-)
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Pfam; PF05885; DICR857; 1.
Pfam; PF00754; F5 F8 type C; 1.
Pfam; PF00746; Zn_CarbOpept; 1.
PRINTS; PR00765; ZRBOXYPTASEA.
SWART; SW00231; PA58C; 1.
PR051TE; PS01285; TASBC; 1.
PR051TE; PS01285; FA58C 1; 1.
PR051TE; PS01286; FA58C 2; UNKNOWN 1.
PR051TE; PS01286; FA58C 2; UNKNOWN 1.
SEQUENCE 845 AA; 96173 MW; 3378DA64C6
  IPR008575; Peptidase_M14B.
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                                                                                                                       - TFYGNVDKDTPVLSELPEPVVARFIRIXPLTW--NGSLCMRLEVLGCPVTPVYSYYAQN 543
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                                  PAEKOETGCPPLGLESLRVSDSRLEASSSQSFGLGPHRGRLNIQSGLEDGDLYDGAWCAE
                                                                                                                                                                544 EVV-TTDSLDFRHHSYKDMRQLMKAVNEECPTITRTYSLGKSSRGLKIYAMEISDNPGDH
                                                                                                                                                                                                                                                         287 PASGSSDPLDFQHHNYKAMRKLMKQVQEQCPNITRIYSIGKSYQGLKLYVMEMSDKPGEH
                                                                                                                                                                                                             NPRSGTFNDFSYLHTNCLELSVYLGCDKFPHESELPREWENNKEALLTFMEQVHRGIKGV
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   Gaps
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"A cDNA cloning of human AEBP1 from primary cultured osteoblasts and its expression in a differentiating osteoblastic cell line.";
EMBL; D86479; BAA13094.1; -...
InterPro; IPR008959; CarboxypepD_reg.
InterPro; IPR008959; CarboxypepD_reg.
InterPro; IPR008979; Gal_Bind_like.
InterPro; IPR008979; Gal_Bind_like.
InterPro; IPR008979; Gal_Bind_like.
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Mammalia, Eutheria, Primates, Catarrhini, Hominidae, Homo.
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TISSUB=Cancellous bone;
MEDLINE=97079196; PubMed=8920928;
Mono I., Hashimoto J., Shimizu K., Takaoka K., Ochi
Okubo K.;
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Last annotation update)
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 75;
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 Conservative
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246;
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                                                                                        Gaps
                                            Query Match 38.0%; Score 1166; DB 2; Length 845;
Best Local Similarity 37.7%; Pred. No. 1.9e-76;
Matches 249; Conservative 74; Mismatches 136; Indels 202;
                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                      467 YYTLPNATVAPETRAVIKWMKRIPFVLSANLHGGELVVSYPFDM------
96173 MW; 3378DA64C413F120 CRC64;
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Last sequence update)
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(TrEMBLrel. 11, I
(TrEMBLrel. 26, I
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01-AUG-1999
01-MAR-2004
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Q14113
ID Q14113
AC Q14113;
DT 01-NOV-1
DT 01-MAR-2
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1054

RC TISSUB=12188257; PubMed=12477932;

RR MEDLINE=22388257; PubMed=12477932;

RA Attacuberg R.L., Collins F.S., Grouse L.H., Derge J.G., unter G.D., Strausberg R.L., Collins F.S., Wagner L., Shenmen C.M., Schuler G.D., Klausner R.D., Collins F.S., Buetow K.H., Schaefer C.F., Bhat N.K., RA Attschul S.F., Zeeberg B. Buetow K.H., Schaefer C.F., Brain G.M., Hong L., Marusina K., Frando M.F., Casavant T.L., Scheetz T.E., Staptchenko L., Marusina K., Frando M.F., Casavant T.L., Scheetz T.E., RA District M.J., Usdin T.B., Toshiyuki S., Carninci P., Mullahy S.J., RA Staple Collins N.J., Peters G.J., Mahek J.A., Mullahy S.J., RA Raha S.S., Loquellano N.A., Peters G.J., Mahek J.A., Hulyk S.W., Rochards S., Worley K.C., Hale S., Garcia A.M., Gay L.J., Hulyk S.W., Willalon D.K., Muzny D.M., Sodergren E.J., Lu X., Gibbs R.A., Richards S., Worley K.C., Hale S., Garcia A.M., Rodrigues S., Sanchez A., Whiting M., Madan A., Young A.C., Shevchenko Y., Boutfard G.G., Whiting M., Madan A., Young A.C., Shevchenko Y., Boutfard G.G., Multing M., I., Skalska U., Smailus D.E., Schnerch A., Schein J.E., Jones S.J., Marra M.A., Randon M., Marra M.A., Randon M., Marra M.A., Sherian D.K., Schein J.S., Jones S.J., Marra M.A., Sherian M.A., Schein J.S., Jones S.J., Marra M.A., Sherian M.A., Sherian M.A., Jones S.J., Marra M.A. 530 BEGPFFCNFVLTKTPKQRLRELLAAGAKVP------PDLR----RRLE---RLRG 571 912 VIDEQGIPIANATISVSGINHGVKTASGGDYWRILNPGEYRVTÄHÄÄGYTPSAKTČNVDY 971 852 NPRTGTINDFSYLHTNCLELSFYLGCDKFPHESELPREWENNKEALLTFWEQVHRGIKGV 911 ...----VTASAEGYHSVTRNCRVTF 529 851 792 ARGEDEDEVSEAQETPDHAIFRWLAISFASAHLTLTEPYRGGCQAQDYTGGMGIVNGAKW Bukaryota; Metazoa; Chordata; Craniata; Vertebrata; Buteleostomi;
Mammalia; Butheria; Primates; Catarrhini; Hominidae; Homo.
NCEI TaxID=9606; Strausberg R.; Submitted (OCT-2002) to the EMBL/GenBank/DDBJ databases. nd mouse cDNA sequences."; roc. Natl. Acad. Sci. U.S.A. 99:16899-16903(2002) 01-MAR-2003 (TrEMBLrel. 23, Created) 01-MAR-2003 (TrEMBLrel. 23, Last sequence update) 01-MAR-2004 (TrEMBLrel. 26, Last annotation update) Adipocyte\_enhancer binding protein 1,. PRT; 1158 AA